REMARKS/ARGUMENTS

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Entry of the claimed amendments is respectfully requested. No new matter is added. Applicant notes with appreciation the Examiner's suggestions in the Official Action mailed January 22, 2002. The Examiner's suggestions were extremely helpful.

Claim 3 has been rejected pursuant to 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner contends that it is unclear if the mammal is suffering from diarrhea which is caused by a pathogenic fungi or not. Applicant has amended claim 3 to clarify that the mammal is suffering from diarrhea which is caused by a pathogenic fungi. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 2-4 have been rejected under 35 U.S.C. § 102(b) as being anticipated by *Hockertz* or *Lodinova-Zadnikova et al.*, or under 35 U.S.C. § 102(a) as anticipated by DE 196 37 936. The Examiner maintains her position that *Hockertz* discloses a one-step administration of DSM 6601 to mice and would inherently prevent diarrhea in these animals. The Examiner also contends that *Lodinova-Zadnikova et al.*, discloses a one-step administration of DSM 6601 to humans and that this administration would inherently prevent fungi-mediated diarrhea. Finally, the Examiner contends that DE 196 37 936 teaches the administration of DSM 6601 and nystatin to treat intestinal *Candida* infection.

At the Examiner's suggestion, Applicant has amended claims 2-4 to indicate that the method is directed to treating or preventing diarrhea mediated by the intestinal colonization of pathogenic fungi in the mammal. In addition, Applicant has

added dependent claims which recite that the method includes administering the DSM 6601 orally (claims 5, 7, and 9) or for at least about 10 days (claims 6, 8 and 10).

Applicant notes that *Hockertz* is directed to the use of DSM 6601 for its ability to enhance the systemic immune response against subsequent systemic infections with pathogenic bacteria or yeast. The prophylactic treatment or therapy of diarrhea caused by bacterial or fungal infections of the intestine by using DSM 6601 is not the subject of this reference. Moreover, the prophylactic effect observed in the reference was dosage-dependent and achieved through a single oral application of DSM 6601 when the causal agent was applied intravenously 24 hours following the prior treatment. Intravenously applied pathogenic agents triggered a systemic infection. No infections of the intestine or associated diarrheas arose in the event. As a result of the different application route, the prophylacticum (*E. coli* DSM 6601) and the causal agent (*Listeria/Candida*) were therefore never in direct contact with each other in the mice. The situation is entirely different to that of an infection of the intestine, where causal agent and preventively or therapeutically applied probioticum are in confrontation with each other within the intestine. Thus, the infection-prophylactic effect in the mouse model used by *Hockertz* is explained solely through the fortifying of the unspecified systemic immune defense. Thus, the contention that the method of *Hockertz* would inherently prevent diarrhea is unfounded. Inherency requires that something necessarily and always happens, and there is absolutely no evidence of that on the record. There is no factual evidence provided to support the legal conclusion of inherency. Therefore, it is improper to merely allege something is inherent and force Applicant to try to prove the negative.

With the respect to the *Lodinova-Zadnikova et al.*

reference, this article merely discloses the administration of the DSM 6601 to newborns and its potential use as a prophylactic for bacterial infections. The issue was the problem of a prophylactic treatment against an undesired colonization in the gastrointestinal tract of newborn babies through germs in their surroundings. The study attempted to solve the question of whether an oral application of DSM 6601 to newborn babies directly following birth might prevent, or at least reduce, a colonization of the gastrointestinal tract with undesired pathogenic bacteria. For this reason, this question was only solved by means of bacteriological stool tests and reports made on the results. There was no search for fungi, nor does the publication make any reference to either fungi in the intestine, diarrhea potentially caused by these or a related therapy. Moreover, none of the children included in the study were sick at the time. The significant reduction of the colonization of undesired bacteria through the intestinal colonization of the children with DSM 6601 demonstrated that the strain possessed antibacterial properties only. Plainly, this reference neither teaches nor suggests that DSM 6601 has anti-fungal activity. Further, there is nothing to suggest that the treatment disclosed in the reference would necessarily and always result in antimycotic activity. Thus, Applicant submits that this reference cannot anticipate the claim methods.

Finally, DE 196 37 936 merely discloses the use of DSM 6601 in combination with the antimycotic nystatin. Again, the *E. coli* strain was used as a bioadhesive for prolonging the retention time of the nystatin at the site of absorption and/or action. In addition, it is noted in the cited specification that the bioadhesive components and effective substance (nystatin) should be combined, chemically or otherwise, with each other. Whether DSM 6601 thus possesses an antimycotic effect of its own is questionable when it is coupled to the

nystatin. The anti-*Candida* effect of DSM 6601 is certainly dependent upon the presence of living, metabolism-active bacteria cells, while the adherence to the intestinal wall is dependent only upon the presence of adhesive cell structures. As such, the method taught in the reference does not necessarily provide anti-fungal activity and is not the "natural result" flowing from the reference's explicit teachings. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

As it is believed that all of the objections and rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

However, if for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that she telephone Applicant's attorney at (908) 654-5000 in order to overcome any additional objections that she might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: June 24, 2002

Respectfully submitted,

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Version With Markings to Show Changes Made

In the Claims

2. (TWICE AMENDED) A method for treating or preventing diarrhea mediated by intestinal colonization of pathogenic fungi in a mammal, comprising administering to the mammal *Escherichia coli* strain DSM 6601.

3. (AMENDED) A method for treating diarrhea mediated by pathogenic fungi in a mammal~~,~~ which suffers from intestinal colonization of the pathogenic fungi, comprising administering to the mammal *Escherichia coli* strain DSM 6601.

4. (AMENDED) A method for preventing diarrhea mediated by intestinal colonization of pathogenic fungi in a mammal, comprising administering to the mammal *Escherichia coli* strain DSM 6601.

5. (NEW) The method of claim 2, wherein the *Escherichia coli* strain DSM 6601 is administered orally.

6. (NEW) The method of claim 2, further comprising administering *Escherichia coli* strain DSM 6601 for at least about 10 days.

7. (NEW) The method of claim 3, wherein the *Escherichia coli* strain DSM 6601 is administered orally.

8. (NEW) The method of claim 3, further comprising administering *Escherichia coli* strain DSM 6601 for at least about 10 days.

9. (NEW) The method of claim 4, wherein the *Escherichia coli* strain DSM 6601 is administered orally.

10. (NEW) The method of claim 4, further comprising administering *Escherichia coli* strain DSM 6601 for at least about 10 days.